Molecular mechanisms of crossing over

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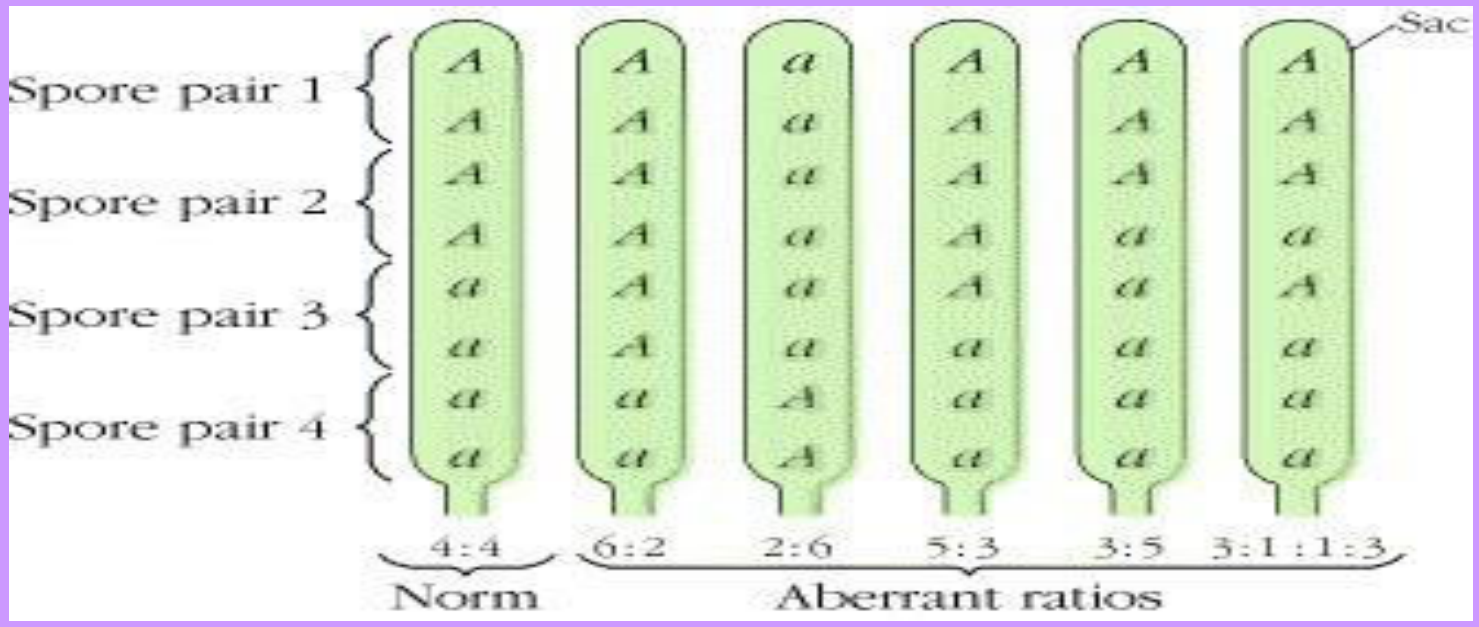
The Mechanism of Crossing-Over - Modern Genetic Analysis

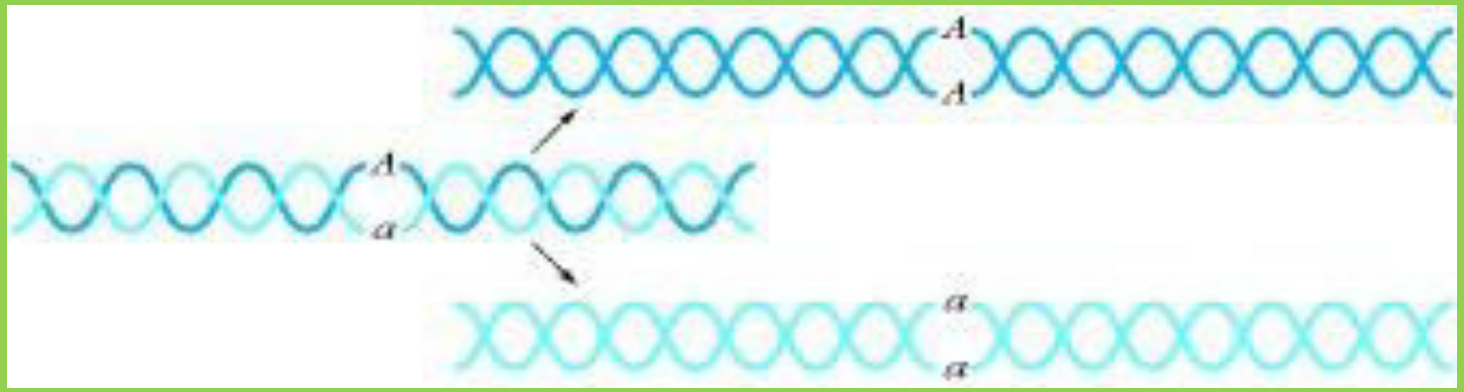
Crossing-over is a remarkably precise process. Some kind of cellular machinery takes two huge molecular assemblages (homologous nonsister chromatids), breaks them in the same relative position, and then rejoins them in a new arrangement so that no genetic material is lost or gained in either. The exact molecular mechanism of crossing-over is not known, but several models have been proposed, and there is general agreement that a key step is the formation of heteroduplex DNA, a hybrid type of DNA molecule that is composed of a strand from one parental chromatid and a strand from the other

Most of the evidence in favor of a heteroduplex model comes from the study of fungal tetrads and octads. Octads are particularly informative in pointing to the existence of heteroduplexes in crossing-over. We have seen in Chapter 4 that in these organisms a cross A × a will create a monohybrid meiocyte A/a that is expected to segregate in a 1:1 ratio in the meiotic products according to the law of equal segregation. Indeed this is found in most meiocytes. In fungi with octads the four nuclei that represent the four products of meiosis undergo an extra mitotic division to produce four ascospore pairs, which stay together in the octad sac.

The expected octad ratio from a monohybrid meiocyte is 4:4. However, in rare meiocytes (generally on the order of 0.1 percent to 1 percent) any one of five types of aberrant ratios can be found, and these gave the clues needed to build a DNA crossover model. The aberrant types are as follows:



All the aberrant ratios need to be explained, but the key types that led to the heteroduplex model are the 5:3, 3:5, and 3:1:1:3 ratios because these contain nonidentical sister spores. (Recall that the postmeiotic round of mitosis is expected to produce identical sister genotypes.) Nonidentical sister spore genotypes must reflect heteroduplex DNA in the meiotic product that gave rise to the pair, that is, DNA with a segment in which one strand is the nucleotide sequence of the A allele and one strand is the nucleotide sequence of the a allele. Upon mitosis the two sister cells resulting from division of such a heteroduplex-containing nucleus will be different, one A and one a.



It has been shown that a Holliday junction can resolve itself in two different ways, involving either a “horizontal” breakage and reunion of the inner two strands at the junction, or a “vertical” breakage and reunion of the outer two strands at the junction. The vertical type produces “genuine” crossover chromatids—that is, whole DNA double-helix crossovers. The horizontal resolution results in a noncrossover conformation. Hence the model suggests that the heteroduplex can be an essential precursor of the genetically detectable chromatid crossover.

Figure 5-18 shows one model of how heteroduplexes might form, the so-called Meselson-Radding model. In the following discussion it is important to refer closely to this figure. A strand from the DNA molecule of one chromatid (blue) breaks, unwinds, and “invades” a nonsister chromatid (yellow). New strand synthesis and joining of broken ends results in a peculiar type of half-helix crossover called a Holliday junction. One of the immediate products is a blue/yellow heteroduplex region. If the Holliday junction migrates by directional unwinding and rewinding of the helix in one direction, then regions are created in which there are two aligned blue/yellow heteroduplexes (shown to the right in the figure).